

In the Specification:

*Please replace paragraph 4 at page 2 of the specification, which continues over to page 3, with the following paragraph:*

To define further the region necessary for the biological activity of the lipocortin N-terminal domain, experiments were carried out where a family of 25 peptides was synthesized in which systematic deletions were made from the N- and C-termini. This enabled a search to be carried out with more precision for the biological active region of the molecule (Croxtall *et al.*, 1998). The results of these studies highlighted the importance of the domain EQEYV (SEQ ID NO:1), as a highly conserved sequence presenting all active peptides. The shortest peptide, which produced significant inhibitory activity, was LC1<sub>18-25</sub> (EQEYVQTV (SEQ ID NO:2)), implying that the domain EQEYV (SEQ ID NO:1), while essential, was not sufficient for biological activity.

*Please replace paragraphs 3-5 at page 3 of the specification with the following paragraphs:*

Surprisingly, it has now been found that the *in vivo* anti-inflammatory properties of LC1 are contained within a different part of the N-terminal amino acid sequence of LC1, specifically LC1<sub>2-6</sub> (N-acetyl LC1<sub>2-6</sub>= AMVSE (SEQ ID NO:3)).

Summary of the Invention

According to the present invention, there is provided a compound comprising the amino acid sequence AMVSE (SEQ ID NO:3), wherein said compound does not comprise the amino acid sequence EQEYVQTV (SEQ ID NO:2).

Also provided by the present invention is a pharmaceutical composition which comprises a compound comprising the amino acid sequence AMVSE (SEQ ID NO:3), wherein said compound does not comprise the amino acid sequence EQEYVQTV (SEQ ID NO:2), and which further comprises one or more pharmaceutically acceptable excipients. Examples of such

excipients include phosphate buffered saline (PBS) at, for example, 0.1 M, pH 7.4, NaHCO<sub>3</sub> at, for example, 0.2 M and other such physiologically acceptable fluids.

*Please replace paragraph 6 at page 3 of the specification, which continues over to page 4, with the following paragraph:*

The present invention also provides the use of a compound comprising the amino acid sequence AMVSE (SEQ ID NO:3), wherein said compound does not comprise the amino acid sequence EQEYVQTV (SEQ ID NO:2), in the manufacture of a medicament for inhibiting leukocyte migration, or treating or preventing inflammation and/or inflammatory response/disease.

*Please replace paragraphs 2-5 at page 4 of the specification with the following paragraphs:*

Yet further provided by the present invention is a method of inhibiting leukocyte migration, or treating or preventing inflammation and/or inflammatory response/disease, comprising administering to an animal an effective amount of a compound comprising the amino acid sequence AMVSE (SEQ ID NO:3), wherein said compound does not comprise the amino acid sequence EQEYVQTV (SEQ ID NO:2).

The present invention may employ any compound comprising the amino acid sequence AMVSE (SEQ ID NO:3) provided it does not comprise the amino acid sequence EQEYVQTV (SEQ ID NO:2). Preferably, the compound is a polypeptide. The polypeptide may be acyclic or cyclic.

The polypeptide may comprise any number of amino acid residues provided that it includes the sequence AMVSE (SEQ ID NO:3) but does not include the sequence EQEYVQTV (SEQ ID NO:2). Preferably, the polypeptide comprises 5-30, preferably 5-20, more preferably 5-11 amino acids. Preferably, the polypeptide comprises AMVSEFLKQAW (SEQ ID NO:4).

The compound may also include additional amino acid sequences or chemical groups flanking the amino acid sequence AMVSE (SEQ ID NO:3), wherein the additional sequences or groups enhance the anti-inflammatory properties of the compound.

*Please replace paragraph 2 at page 5 of the specification with the following paragraph:*

The present invention also provides the method as described above, wherein a composition which comprises a compound comprising the amino acid sequence AMVSE (SEQ ID NO:3), wherein said compound does not comprise the amino acid sequence EQEYVQTV (SEQ ID NO:2), and which further comprises one or more pharmaceutically acceptable excipients is administered to an animal.

*Please replace paragraphs 4-5 at page 5 of the specification with the following paragraphs:*

**Figure 1** illustrates the degree of inflammatory response (as measured by PMN migration) generated by the *in vivo* activity of lipocortin 1-derived peptides (Scramble = LC<sub>1-6</sub> (Ac-SVEMA (SEQ ID NO:5)); Ac=acetyl).

**Figure 2** illustrates (as a bar chart) the degree of inflammatory response (as measured by PMN migration) generated by the *in vivo* activity of 66 nmol lipocortin 1-derived peptides with reference to Figure 1 (Scramble = LC<sub>1-6</sub> (Ac-SVEMA (SEQ ID NO:5)); Ac=acetyl).

*Please replace paragraph 6 at page 5 of the specification, which continues over to page 6, with the following paragraph:*

The *in vivo* anti-inflammatory properties of the amino acid sequence AMVSE (SEQ ID NO:3) were demonstrated by preparing fragments of N-acetyl LC<sub>1-26</sub> (AMVSEFLKQAWFIENEEQEYVQTVK (SEQ ID NO:6)) and testing them in an animal model of inflammation. The *in vivo* animal model provided evidence that while N-acetyl LC<sub>1-12</sub> (AMVSEFLKQAW (SEQ ID NO:4)) was active in the model, LC<sub>1-13-25</sub> (FIENEEQEYVQTV

(SEQ ID NO:7)) was not (data not shown). When AMVSE (SEQ ID NO:3) and LC1<sub>7-12</sub> (FLKQAW (SEQ ID NO:8)), were tested the former was active whereas the latter was not. A scrambled version of AMVSE (SEQ ID NO:3) (namely, SVEMA (SEQ ID NO:5)) was also found to be inactive.

*Please replace paragraph 2 at page 9 of the specification with the following paragraph:*

*Drug Treatment*

The following peptides were drawn from the lipocortin 1 N-terminus region: LC1<sub>2-26</sub> (Ac-AMVSEFLKQAWFIENEEQEYVQTVK (SEQ ID NO:6)), LC1<sub>2-12</sub> (Ac-AMVSEFLKQAW (SEQ ID NO:4)), LC1<sub>13-25</sub> (FIENEEQEYVQTV (SEQ ID NO:7)), LC1<sub>2-6</sub> (Ac-AMVSE (SEQ ID NO:3))), or scramble LC1<sub>2-6</sub> (Ac-SVEMA (SEQ ID NO:5)) were administered s.c. 30 min prior to injection of 1 mg zymosan into the air-pouches. Control mice were treated with sterile PBS (100  $\mu$ l s.c.).

*Please replace paragraph 4 at page 9 of the specification with the following paragraph:*

LC1<sub>2-26</sub> itself showed the greatest potency. This is likely to be due to the presence of residues flanking the AMVSE (SEQ ID NO:3) sequence that increase the PMN migration inhibitory activity of the pharmacore AMVSE (SEQ ID NO:3).

*Please replace paragraph 6 at page 9 of the specification, which continues over to page 10, with the following paragraph:*

The results clearly indicate the inhibitory effect of the AMVSE (SEQ ID NO:3) pharmacore on PMN migration and the possibility of its enhanced potency in combination with suitable flanking sequences. The AMVSE (SEQ ID NO:3) pharmacore represents the minimum active sequence from which further useful sequences may be derived by combining the core AMVSE (SEQ ID NO:3) sequence with additional flanking sequences, chemical groups designed to improve the binding or penetration of the peptide to its active site or other chemical groups that in some other

way improve the anti-inflammatory properties of a compound comprising the pharmacore **AMVSE (SEQ ID NO:3)**.

*Please replace paragraph 1 at page 13 of the specification with the following paragraph:*

#### ABSTRACT

A compound comprising the amino acid sequence **AMVSE (SEQ ID NO:3)**, wherein said compound does not comprise the amino acid sequence **EQEYVQTV (SEQ ID NO:2)**. The compound is useful as an anti-inflammatory agent.

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